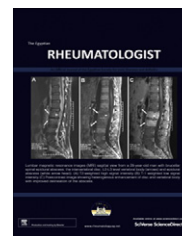




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ORIGINAL ARTICLE

Brucellar spinal epidural abscesses. Single center experience of nineteen patients and review of the literature

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KEYWORDS

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Abstract *Objective:* Brucellar spinal epidural abscesses (SEA) are rare and very few series of them have been reported. We aimed to evaluate the clinical characteristics, laboratory, radiological findings and outcome of this entity.

Methods: Of 146 patients with brucellosis, 19 (13%) patients were diagnosed to have SEA during a period of 21 years (1990–2010). Diagnosis made on clinical presentation, laboratory findings, radiographic evidence and the brucellar etiology was considered when seroagglutination tests were positive at a titer of 1/160 or higher, and/or *Brucella* spp. were isolated in the blood.

Results: The mean age of patients was 51 ± 16 years (14 males, 5 females; age range, 22–74 years). The median diagnostic delay was 2 months. Back or neck pain (100% of patients), fever (100%), and sweating (68.6%) were the most common symptoms. Cultures of blood specimens from 4 patients (21%) were positive for *Brucella melitensis*. Three patients (15.8%) had motor weakness or paralysis. Magnetic resonance imaging was performed in all cases. The lumbar vertebra was the most frequently involved region with the rate of 84.2%, followed by thoracic (15.8%), cervical (5.3%), lumbosacral (5.3%), and thoraco–lumbar (5.3%) segments. A combination of rifampin and doxycycline was the most widely used therapy regimen (9 cases, 47.3%). The duration of antimicrobial therapy of brucellosis (median, 7 months; range, 4–13 months) varied according to the clinical response. There were no deaths or severe sequelae in this study.

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Conclusion: Brucellar SEA should be considered in patients who have back pain and neurologic disorders as well as systemic symptoms and findings in or from endemic areas.

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1. Introduction

Brucellosis, a zoonosis with worldwide distribution, is a systemic infection caused by facultative intracellular bacteria of the genus *Brucella*, which can involve multiple organs [1]. *Brucella melitensis* is the most virulent and most widely encountered of all the species. *Brucella* may enter the host via ingestion or inhalation, or through conjunctiva or skin abrasions. Humans are infected by direct contact with animals, animal tissues (especially placenta) or by the ingestion of animal products (milk or dairy) that are contaminated with the *Brucella* bacteria [2]. The symptoms of brucellosis are non-specific such as osteoarticular complaints, fatigue, sweating, prolonged fever, anxiety or depression, and hepatobiliary or gastrointestinal abnormalities. Sacroiliitis, arthritis, osteomyelitis and spondylodiscitis are the most common complications of brucellosis, and spondylitis is the most prevalent and important clinical form of osteoarticular involvement [3]. Brucellar spinal epidural abscesses (SEA) are rare and very few series of them have been reported [4–8]. We aimed to evaluate the clinical characteristics, laboratory, radiological findings and outcome of this entity.

2. Patients and methods

It was a retrospective study performed in the Infectious Diseases department of Sfax (south of Tunisia) between 1990 and 2010. Of 145 patients with brucellosis, 19 (13%) patients were diagnosed to have Brucellar SEA. No patient had evidence of tuberculosis infection (negative intradermal tuberculin test, normal chest X-ray and sputum culture results come back negative). The following laboratory tests were performed: Rose Bengal test, standard tube agglutination testing, complete blood count, C-reactive protein, and erythrocyte sedimentation rate. A diagnosis of brucellosis was established by history, physical examination, serologic analysis ($\geq 1/160$ titers of *brucella* agglutination tests) or isolation of bacteria from blood or sample cultures. Conventional methods were used for the identification of the *Brucella* species [9]. Spinal magnetic resonance imaging (MRI) was used in 19 cases (100%), whereas 14 patients were evaluated with a computed tomography (CT) scan. For treatment, we used a combination of doxycycline and rifampin because of the risk of toxicity with aminoglycosides. In some cases we added ofloxacin or trimethoprim-sulfamethoxazole because of their excellent bone diffusion. The response to therapy was evaluated by performing radiographic, clinical, and laboratory examinations before and after therapy. Antibiotics were not discontinued until there was a clear improvement of clinical and radiological findings.

3. Results

The mean age of patients was 51 ± 16 years (14 males, 5 females; age range, 22–74 years). All the cases were from the

south of Tunisia. The symptoms and clinical findings are shown in Table 1. The time from the onset of symptoms to diagnosis of Brucellar SEA was 1–7 (median, 2) months. The ingestion of nonpasteurized milk or milk products of infected cows (19 cases, 100%) and contact with infected animals (16 cases, 84.2%) are the main risk factors of human brucellosis in this study.

Erythrocyte sedimentation rates were measured for 19 patients, which ranged from 5 to 115 mm/h (mean, 55 ± 28 mm/h) and three patients had a normal rate. C-reactive protein levels were measured in 15 patients (median, 55 mg/L; range, 5–199 mg/L), only one patient had normal values. Leukopenia (< 4000 WBCs/mm³) was found in 3 patients (15.8%). Anemia (hemoglobin concentration < 12 g/dL) was found in 5 patients (26.3%). All of the patients were positive for the Rose Bengal test. Standard tube agglutination testing of initial samples (before the onset of treatment) from the 19 patients (100%) was positive for antibodies to *Brucella* (titer, $\geq 1/160$). Blood cultures were positive for 4 patients for whom these titers were $> 1/160$. Disco-vertebral needle biopsies are realized in 8 (42.1%) of 19 cases. Only 1 specimen (12.5%) has shown a brucellian granuloma. All CT-guided needle biopsy cultures were negative.

All patients underwent MRI at least once. CT scans of the spine were obtained in 14 (73.7%) cases. At admission 19 patients showed signs of spondylodiscitis of adjacent to the SEA in MRI and/or CT studies. All patients had involvement of only a single spinal region. Two patients had contiguous involvement at multiple levels (> 2 vertebral bodies). Thirteen (68%) patients had diffuse hyperintensity of the vertebral body at MRI in T2 sequences. The lumbar vertebra was the most frequently involved region with the rate of 84.2% particularly at the level of the L4/L5 vertebra, followed by thoracic (15.8%), cervical (5.3%), lumbosacral (5.3%), and thoracolumbar (5.3%) segments (Table 2). Only one patient had another focus other than the spine in the left sacroiliac joint. MRI examination revealed an extradural soft tissue mass. They were iso- to hypointense compared to the spinal cord

Table 1 Clinical features at presentation of 19 patients with brucellar spinal epidural abscesses.

Symptoms and clinical findings	n (%)
Back pain	19 (100)
Fever ≥ 38 °C	19 (100)
Sweating	13 (68.4)
Weight loss	7 (36.8)
Weakness or fatigue	6 (31.6)
Arthralgia	6 (31.6)
Motor weakness	3 (15.8)
Myalgia	2 (10.5)
Splenomegaly	2 (15.5)
Hepatomegaly	1 (5.3)
Sacroiliac pain	1 (5.3)

Table 2 Clinical, laboratory features and treatment for 19 patients with brucellar spinal epidural abscesses.

Patient no.	Age/sex	Level	Neurological involvement	Sphincter affected	Serology ^a	Blood culture	Treatment (months)
1	58/M	C4-C5	Hypoesthesia of the right upper extremity	—	1/1280	+	R + D + T-S (7)
2	53/M	D7-D8	—	—	1/320	—	R + D + T-S (6)
3	57/M	D10-D11	Weakness in lower limbs	+	1/320	—	R + T (13)
4	64/M	D12-L1	Motor weakness in right leg	—	1/320	—	R + D (4)
5	74/M	L1-L2	Hypoesthesia of the legs	—	1/640	+	R + T (6)
6	28/M	L2-L3	—	—	1/160	—	R + D (5)
7	65/F	L2-L3-L4	—	—	1/640	—	R + D + T-S (9)
8	63/M	L2-L3-L4	—	—	1/640	+	R + D + T-S (12)
9	32/M	L3-L4	—	—	1/1280	+	R + D (6)
10	34/F	L3-L4	Motor weakness in right lower limb	—	1/160	—	R + D (4)
11	68/F	L4-L5	—	—	1/1280	—	R + D (6)
12	56/M	L4-L5	Hypoesthesia of the left lower limb	—	1/320	—	R + D + T-S (9)
13	34/M	L4-L5	Hypoesthesia of the left thigh	—	1/640	—	R + D + T-S (11)
14	54/M	L4-L5	—	—	1/640	—	R + D (10)
15	46/F	L4-L5	Pain in lower limbs	—	1/640	—	R + D + O (10)
16	28/M	L4-L5	—	—	1/640	—	R + D + T-S (6)
17	64/M	L4-L5	—	—	1/1280	—	R + D + T-S (9)
18	67/F	L4-L5	—	—	1/640	—	R + D (7)
19	22/M	L5-S1	Right sciatica	—	1/640	—	R + D + O (10)

M, male; F, female; D, doxycycline; T, tetracycline; R, rifampicin; O, ofloxacin; T-S, trimethoprim-sulfamethoxazole.

^a Standard agglutination test.

on T1 and hyperintense on T2-weighted images. Following contrast administration, diffusely homogeneous or slightly heterogeneous enhancement was seen with thick or thin enhancement surrounding a liquified low signal pus collection (Fig. 1).

All patients received antibiotic treatment with a combination of 2 (9 patients, 47.3%) or 3 (10 patients, 52.6%) agents. Nine patients (47.3%) received a combination of tetracycline (especially doxycycline: 200 mg/day orally) and rifampin (900 mg/day orally). Eight patients (42.1%) received a combination of doxycycline (200 mg/day orally), rifampin (900 mg/day orally) and trimethoprim-sulfamethoxazole. Two patients (10.5%) received a combination of doxycycline (200 mg/day orally), rifampin (900 mg/day orally) and ofloxacin (Table 2). The mean duration of the antimicrobial treatment was 7.9 ± 2.6 months (range, 4–13 months) and 11 (57.9%) of the patients received therapy for > 6 months. None of the patients needed surgery and all favorably responded to medical treatments.

Our cases responded well to the medical treatment. The period of defervescence at the beginning of therapy was between 6 and 23 days (median, 7 days). All patients were available for follow-up for at least 15 months (median, 45 months). Soft tissue lesions were almost totally cured. Seventeen patients had rapid regression of symptoms. No motor sequelae were observed at last follow-up in all patients. Nonsteroidal anti-inflammatory drugs were administered for two patients for back pain.

4. Discussion

Human brucellosis remains an important public health problem [10]. Rheumatic complaints are seen in 20–85% of the patients [11,12]. Bone involvement in brucellosis ranges from 2% to 70%. The spine is the most common site of bony brucellosis [13]. Brucellar SEA are rarely described in the literature, and most of them are reported as single cases. The present series is the largest patient group reported regarding brucellar SEA

in the literature. By searching in Pub Med, we have been able to find five reports of case-series [4–8]. (Table 3)

The clinical manifestations of epidural abscess consist of prominent spinal pain, local tenderness and fever; however, the pain may be absent in 10–15% of cases and fever in half the cases [14,15]. In our study, the mean age of patients was 51 ± 16 years, which accords with reports from other authors [4,6]. Most patients in this study were male, lived in rural areas, and had occupational risk factors, whereas in the studies from Spain [6] and Turkey [5], the disease predominated in females and was mainly caused by the ingestion of unpasteurized dairy products. In our study, 15% of the patients had a severe motor deficit or paralysis at diagnosis which represents the lowest rate compared to other series (Table 3). The time from the onset of symptoms to diagnosis of SEA was between 1 and 9 months comparable with other studies [4,5]. Because a clear relation exists between delayed diagnosis and the presence of more-destructive lesions and neurological deficit, brucellar SEA should be considered in any adult patient with brucellosis who has inflammatory spinal pain or paravertebral tenderness [4,16].

Abnormal results of blood tests are usually non specific. The hemoglobin level may be lowered as a result of prolonged infection, and a moderately elevated erythrocyte sedimentation rate is found in most cases [15]. Rose-Bengal shows rapid agglutination, and it can be used as a screening test [17]. When brucellosis is suspected, detection of high or rising titers of specific antibodies to *Brucella* (≥ 160 , standard tube agglutination test) in the serum helps a presumptive diagnosis [9]. Standard *Brucella* tube agglutination testing of initial samples for all patients was $\geq 1:160$ for antibodies to *Brucella* species (Table 2). The finding of *Brucella* organisms in blood culture is the conclusive diagnostic [18].

Brucellar spondylodiscitis generally arises from the upper end plate where the blood supply is rich, and it may spread to the whole vertebra, discolor space and adjacent vertebrae, depending on the virulence of the micro-organism, the size of the inoculum and the immune status of the host [5]. Therefore,

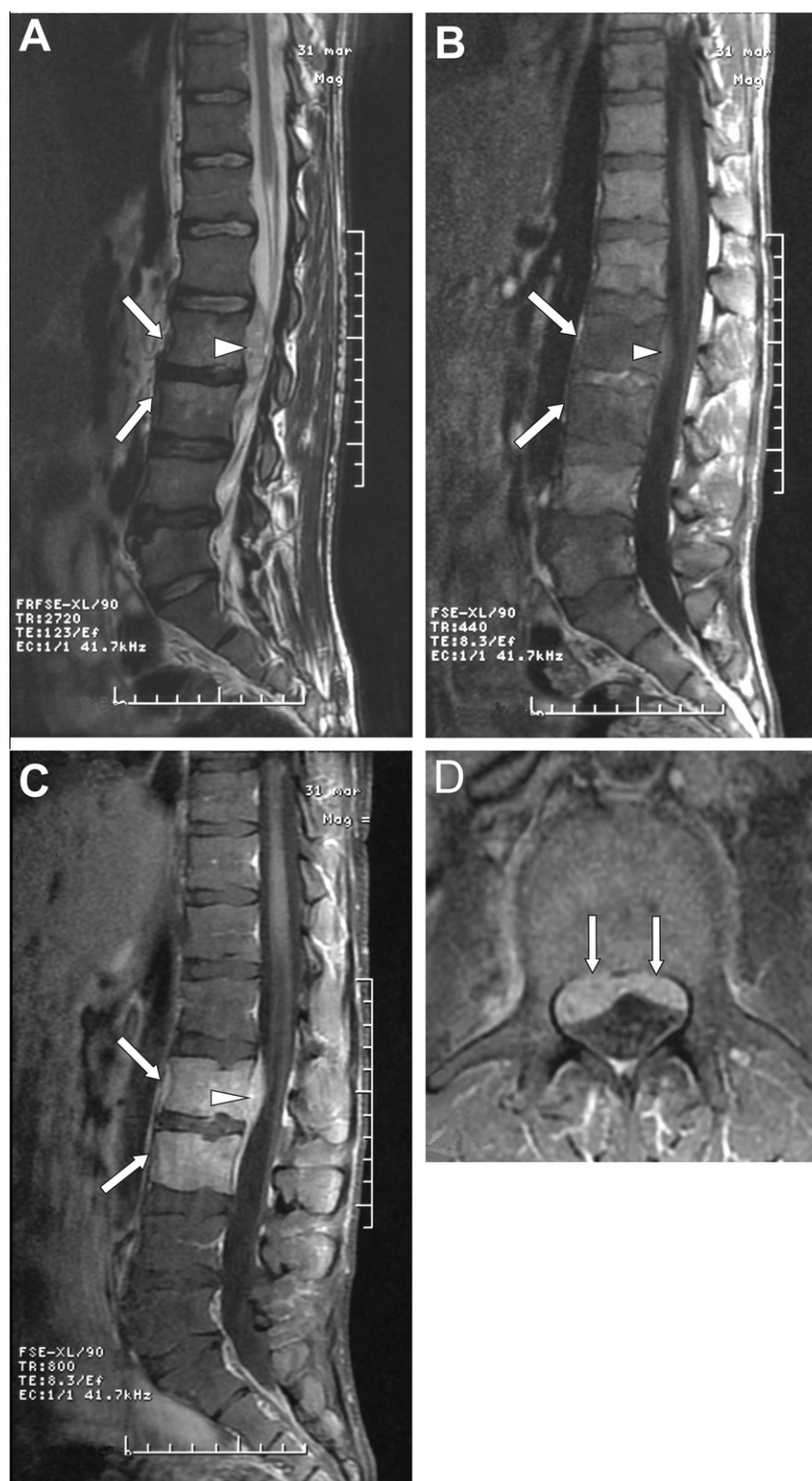


Figure 1 (Patient no. 6) lumbar magnetic resonance images from a 28-year-old man with brucellar spinal epidural abscess. (A) T2-weighted sagittal image showing high signal intensity of the intervertebral discolor, vertebral body at the L2-L3 level (arrow) and epidural abscess (white arrowhead). (B) T1-weighted sagittal image showing low signal intensity of the intervertebral discolor, vertebral body (arrow) and epidural abscess (white arrowhead). (C) In the postcontrast image, heterogenous enhancement of discolor and adjacent vertebral body of L2 and L3 (arrow) was seen and epidural abscess (white arrowhead) is better delineated. (D) Postcontrast T1-weighted axial image showing the diffuse enhancement in the L2 body and epidural abscess is also seen (arrow).

Table 3 Summary of all reported case-series of brucellar spinal epidural abscess.

References	Country	Number of cases	Sex ratio ^a	Mean of age (years)	Vertebral involvement (n)	Motor weakness ^a (%)	Treatment (weeks) ^b	Surgery (n)
Pina [6]	Spain	4	0.33	53.5	C (4)	25	19	4
Ozates [7]	Turkey	6	1	37	L (6), S (1)	50	NL	NL
Faria [8]	Portugal	9	1.25	49	C (4), T (5)	88.8	NL	8
Gorgulu [5]	Turkey	9	0.5	62.5	C (1), T (3) L (6), S (2)	33.3	8.5	1
Ugariza [4]	Spain	11	1.75	47.7	C (3), T (4) L (5), S (3)	36.3	8.1	6
Our serie	Tunisia	19	2.8	51	C (1), T (3) L (16), S (1)	15.7	32	0

C, cervical; T, thoracic; L, lumbar; S, sacrum; n, number of patients; μ , male/female ratio; NL, not listed.

^a At presentation.

^b Mean duration.

brucellar SEA mostly results from direct invasion followed by spondylitis [16]. However, very rarely, it may develop via a direct hematogenous route without spondylitis [5,6]. The lumbar spine is the most frequent level involved, followed by the thoracic and the cervical segments [13,16,19]. In our series, the lumbar segment was also the most frequently involved region with a rate of 84.2% particularly at the level of the L4/L5 vertebra. MRI is considered to be the gold standard for the diagnosis of SEA. Spinal brucellosis may be focal or diffuse. Focal Brucellar spondylodiscitis appears as focal areas of abnormal signal intensity and is usually localized in the anterior aspect of an end plate of a vertebra at the discovertebral junction. Diffuse form of Brucellar spondylodiscitis is defined as diffuse abnormal signal intensity in the adjacent vertebra and the intervening disk. Epidural abscess is seen as a mass lesion within the spinal canal and outside to the spinal cord, hyperintense on T2-weighted, and slightly hypointense on T1-weighted MRI. Abscess is better delineated with contrast enhancement with Gd-DTPA [18,20]. CT scanning may be applicable and useful for the detection of bony changes in the spine [16,18].

Diverse treatment options for spinal brucellosis have been reported in the literature and good results have been obtained with antibiotic therapy alone [4,16,21]. There is still no consensus in choosing the appropriate antibiotics and the treatment duration in patients with Brucellar SEA [6,22]. A combination of doxycycline with streptomycin is still the first line antimicrobial regimen in spinal brucellosis. Doxycycline + rifampin or trimethoprim-sulfamethoxazole + rifampin or ciprofloxacin + rifampin or ciprofloxacin + streptomycin could be used as an alternative when adverse reactions or contraindications are present [22]. It is also recommended that antibiotic therapy should be prolonged up to 6 weeks to 1 year in patients with brucellar SEA [5,6,23]. Surgical treatment is indicated whenever a root, spinal cord or dura mater compression is seen on MRI, spinal instability, an anterior abscess larger than 2.5 cm or unsuccessful medical treatment [24,25]. Some authors reported good results in patients who underwent surgery plus antibiotic therapy [6,26]. In our series, antimicrobial therapy was preferentially considered over surgical decompression. No relapse or sequelae were observed. Our results are in marked contrast to those of Faria [8], Ozates [7] and Ugariza [4] who reported that many of their patients (36.3–88.8%) were

in need of surgical treatment. This might be due to the high incidence of thoracic and cervical SEA in their series.

In conclusion, Brucellar SEA should be considered in patients who have back pain and neurologic disorders as well as systemic symptoms and findings in or from endemic areas. Antibiotic therapy could be primary treatment in brucellar SEA and is effective in many patients. Brucellar SEA has a good prognosis with early diagnosis and appropriate management.

5. Conflict of interest statement

There is no conflict of interest of the authors.

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